

FORM PTO-1449		<div style="border: 1px solid black; border-radius: 50%; padding: 10px; display: inline-block;"> <b>UIPE</b>  <b>MAR 05 2002</b>  <b>PATENT &amp; TRADEMARK</b> </div>		ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
INFORMATION DISCLOSURE STATEMENT				<b>MAR 06 2002</b>		<b>TECH CENTER 1600/2900</b>	
				APPLICANT Bush et al.		FILING DATE September 21, 2001	
				GROUP 1614			

PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
KW	AA1	5,110,493	05/05/1992	Cherng-Chyi et al.	514	413	12/07/1990
	AB1	5,242,932	09/07/1993	Gandy et al.	514	313	12/17/1991
	AC1	5,357,636	10/25/1994	Dresdner, Jr. et al.	2	161.7	06/30/1992
	AD1	5,373,021	12/13/1994	Marangos	514	483	04/26/1993
	AE1	5,466,680	11/14/1995	Rudy	514	57	03/26/1992
	AF1	5,523,295	06/04/1996	Fasman	514	63	07/06/1994
	AG1	5,688,516	11/18/1997	Raad et al.	424	409	10/03/1994
	AH1	5,688,651	11/18/1997	Solomon	435	7.1	12/16/1994
	AI1	5,705,401	01/06/1998	Masters et al.	436	518	09/16/1994
	AJ1	5,707,821	01/13/1998	Rydel et al.	435	18	06/07/1995
KW	AK1	5,721,106	02/24/1998	Maggio et al.	435	7.8	09/12/1994

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
KW	AL1	WO 92/18111	10/29/1992	WIPO	—	—	Yes No
	AM1	WO 93/10459	05/27/1993	WIPO	—	—	Yes No
	AN1	WO 93/24451	12/09/1993	WIPO	—	—	Yes No
	AO1	WO 94/04167	03/03/1994	WIPO	—	—	Yes No
KW	AP1	WO 95/31199	11/23/1995	WIPO	—	—	Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KW	AR	1	Assaf, S.Y and Chung, S.-H., "Release of endogenous Zn <sup>2+</sup> from brain tissue during activity," <i>Nature</i> 308:734-736, Macmillan Journals Ltd. (1984).
KW	AS	1	Atwood, C.S., et al., "Copper-Mediated Aggregation And Polymerization of Aβ," <i>Soc. Neurosci. Abstr.</i> 23:1883, Abstr. No. 731.9, Society for Neuroscience (October 1997).
KW	AT	1	Atwood, C.S., et al., "Dramatic Aggregation of Alzheimer Aβ by Cu(II) Is Induced by Conditions Representing Physiological Acidosis," <i>J. Biol. Chem.</i> 273:12817-12826, The American Society for Biochemistry and Molecular Biology, Inc. (May 1998).

EXAMINER KW. Wedderburn	DATE CONSIDERED 6-16-02
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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET AND MARK OFFICE  
0609.45500017JAG/FRCAPPLICATION NO.  
09/956,980APPLICANT  
Bush et al.FILING DATE  
September 21, 2001GROUP  
1614

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## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
lw	AA2	5,927,283	07/27/1999	Abraham et al.	128	898	05/08/1997
	AB2	5,980,914	11/09/1999	Gerolymatos	424	400	02/13/1998
	AC2	5,994,323	11/30/1999	Gerolymatos	514	52	02/13/1998
	AD2	6,001,852	12/14/1999	Gerolymatos	514	311	02/13/1998
lw	AE2	6,323,218 B1	11/27/2001	Bush et al.	514	311	03/11/1998
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## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
lw	AL2	WO 96/07096	03/07/1996	WIPO	—	—	Yes No
	AM2	WO 96/12544	05/02/1996	WIPO	—	—	Yes No
	AN2	WO 96/28471	09/19/1996	WIPO	—	—	Yes No
	AO2	WO 97/04794	02/13/1997	WIPO	—	—	Yes No
lw	AP2	WO 97/09976 A2	03/20/1997	WIPO	—	—	Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

lw	AR	2	Atwood, C.S., et al., "Role of Free Radicals and Metal Ions in the Pathogenesis of Alzheimer's Disease," in: <i>Metal Ions in Biological Systems</i> , vol. 36, Ch. 10, Sigel, A. and Sigel, H., eds., Marcel Dekker, Inc., New York, New York, pp. 309-364 (March 1999).
lw	AS	2	Bacon, P.A., et al., "Rheumatoid Disease, Amyloidosis and its Treatment with Penicillamine," <i>Eur. J. Rheum. Inflamm.</i> 2:70-74, Cameron Publishers (1979).
lw	AT	2	Barrow, C.J. and Zagorski, M.G., "Solution Structures of $\beta$ Peptide and Its Constituent Fragments: Relation to Amyloid Deposition," <i>Science</i> 253:179-182, American Association for the Advancement of Science (1991).

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	APPLICANT Bush et al.	
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W	AL3	WO 97/09976 A3	03/20/1997	WIPO	—	—	Yes No
I	AM3	WO 97/36885	10/09/1997	WIPO	—	—	Yes No
I	AN3	WO 98/06403	02/19/1998	WIPO	—	—	Yes No
	AO3	WO 98/40071	09/17/1998	WIPO	—	—	Yes No
W	AP3	WO 99/09981	03/04/1999	WIPO	—	—	Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

W	AR	3	Barrow, C.J., et al., "Solution Conformations and Aggregational Properties of Synthetic Amyloid $\beta$ -Peptides of Alzheimer's Disease," <i>J. Mol. Biol.</i> 225:1075-1093, Academic Press Limited (1992).
I	AS	3	Basun, H., et al., "Metals and trace elements in plasma and cerebrospinal fluid in normal ageing and Alzheimer's disease," <i>J. Neural Transm. [P-D Sect.]</i> 4:231-258, Springer-Verlag (1991).
W	AT	3	Beal, M.F., "Energy, Oxidative Damage, and Alzheimer's Disease: Clues to the Underlying Puzzle," <i>Neurobiol. Aging</i> 15:S171-S174, Elsevier Science Ltd. (1994).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
ll	AL4	WO 99/18432	04/15/1999	WIPO	—	—	Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

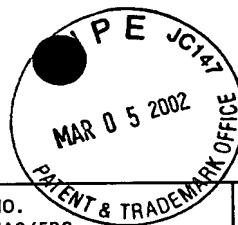
lc	AR	4	Behl, C., et al., "Hydrogen Peroxide Mediates Amyloid $\beta$ Protein Toxicity," <i>Cell</i> 77:817-827, Cell Press (1994).
l	AS	4	Biaglow, J.E. and Kachur, A.V., "The Generation of Hydroxyl Radicals in the Reaction of Molecular Oxygen with Polyphosphate Complexes of Ferrous Ion," <i>Radiation Res.</i> 148:181-187, Radiation Research Society (August 1997).
ll	AT	4	Boado, R.J., et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>J. Pharm. Sci.</i> 87:1308-1315, The American Pharmaceutical Association and The American Chemical Society (November 1998).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

ke	AR	5	Borman, S., "Diverse Strategies Emerge For Diagnosing Alzheimer's Disease," <i>Chem. Eng. News</i> 272:33-34, The American Chemical Society (1996).
I	AS	5	Bruce, A.J., <i>et al.</i> , " $\beta$ -Amyloid toxicity in organotypic hippocampal cultures: Protection by EUK-8, a synthetic catalytic free radical scavenger," <i>Proc. Natl. Acad. Sci. USA</i> 93:2312-2316, National Academy of Sciences (1996).
ke	AT	5	Bruijn, L.I., <i>et al.</i> , "ALS-Linked SOD1 Mutant G85R Mediates Damage to Astrocytes and Promotes Rapidly Progressive Disease with SOD1-Containing Inclusions," <i>Neuron</i> 18:327-338, Cell Press (February 1997).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

W	AR	6	Burdick, D., <i>et al.</i> , "Assembly and Aggregation Properties of Synthetic Alzheimer's A4/ $\beta$ Amyloid Peptide Analogs," <i>J. Biol. Chem.</i> 267:546-554, The American Society for Biochemistry and Molecular Biology, Inc. (1992).
I	AS	6	Burns, J.A., <i>et al.</i> , "Selective Reduction of Disulfides by Tris(2-carboxyethyl)phosphine," <i>J. Org. Chem.</i> 56:2648-2650, The American Chemical Society (1991).
W	AT	6	Busciglio, J. and Yankner, B.A., "Apoptosis and increased generation of reactive oxygen species in Down's Syndrome neurons <i>in vitro</i> ," <i>Nature</i> 378:776-779, Macmillan Journals Ltd. (1995).

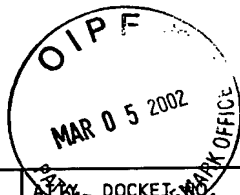
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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

APPL. DOCKET NO.  
0609-165500 JAG/FRCAPPLICATION NO.  
09/956,985APPLICANT  
Bush et al.FILING DATE  
September 21, 2001GROUP  
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## U.S. PATENT DOCUMENTS

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	AP						Yes No

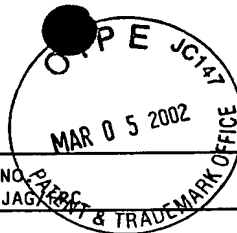
## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

lc	AR	Z	Bush, A.I., et al., "A Novel Zinc(II) Binding Site Modulates the Function of the $\beta$ A4 Amyloid Protein Precursor of Alzheimer's Disease," <i>J. Biol. Chem.</i> 268:16109-16112, The American Society for Biochemistry and Molecular Biology, Inc. (1993).
I	AS	Z	Bush, A.I., et al., "Modulation of A $\beta$ Adhesiveness and Secretase Site Cleavage by Zinc," <i>J. Biol. Chem.</i> 269:12152-12158, The American Society for Biochemistry and Molecular Biology, Inc. (1994).
lc	AT	Z	Bush, A.I., et al., "Rapid Induction of Alzheimer A $\beta$ Amyloid Formation by Zinc," <i>Science</i> 265: 1464-1467, American Association for the Advancement of Science (1994).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

lc	AR	8	Bush, A.I., <i>et al.</i> , "The Amyloid $\beta$ -Protein Precursor and Its Mammalian Homologues," <i>J. Biol. Chem.</i> 269:26618-26621, The American Society for Biochemistry and Molecular Biology, Inc. (1994).
1	AS	8	Bush, A.I., <i>et al.</i> , "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1923, American Association for the Advancement of Science (1995).
ll	AT	8	Butterfield, D.A., <i>et al.</i> , " $\beta$ -Amyloid Peptide Free Radical Fragments Initiate Synaptosomal Lipoperoxidation in a Sequence-Specific Fashion: Implications to Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 200:710-715, Academic Press, Inc. (1994).

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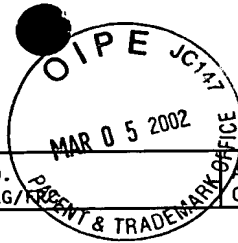
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INFORMATION DISCLOSURE STATEMENTATTY. DOCKET NO.  
0609.4550001/JAG/RECENT & TRADEMARK OFFICEAPPLICATION NO.  
09/956,980APPLICANT  
Bush et al.FILING DATE  
September 21, 2001GROUP  
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## U.S. PATENT DOCUMENTS

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	AL						Yes No
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	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

cc	AR	2	Butterfield, D.A., et al., "A $\beta$ (25-35) Peptide Displays H <sub>2</sub> O <sub>2</sub> -Like Reactivity Towards Aqueous Fe <sup>2+</sup> , Nitroxide Spin Probes, and Synaptosomal Membrane Proteins," <i>Life Sci.</i> 58:217-228, Elsevier Science Inc. (1996).
	AS	2	Ceballos-Picot, I., et al., "Peripheral Antioxidant Enzyme Activities And Selenium In Elderly Subjects And In Dementia Of Alzheimer's Type-Place Of The Extracellular Glutathione Peroxidase," <i>Free Radic. Biol. Med.</i> 20:579-587, Elsevier Science Inc. (1996).
cc	AT	2	Cherny, R.A., et al., "The Aggregation of A $\beta$ in Human Brain is Mediated by Zinc," <i>Soc. Neurosci. Abstr.</i> 23:534, Abstract 209.6, Society for Neuroscience (October 1997).

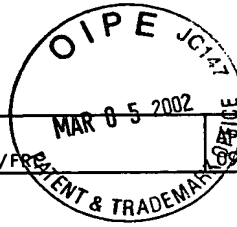
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	AM						Yes No
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	AO						Yes No
	AP						Yes No

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11C	AR	10	Chong, Y.-H and Suh, Y.-H., "Aggregation of amyloid precursor proteins by aluminum in vitro," <i>Brain Res.</i> 670:137-141, Elsevier Science B.V. (1995).
1	AS	10	Cohen, A.S., "Amyloidosis," in: <i>Arthritis and Allied Conditions- A Textbook of Rheumatology</i> , D.J. McCarty, ed., Lea and Febiger, Philadelphia, Pennsylvania, pp. 1273-1293 (1989).
10	AT	10	Colaco, C.A.L.S., et al., "The role of the Maillard reaction in other pathologies: Alzheimer's disease," <i>Nephrol. Dial. Transplant.</i> 11(Suppl. 5):7-12, Oxford University Press (1996).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

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60	AR	11	Connor, J.R., <i>et al.</i> , "A Histochemical Study of Iron, Transferrin, and Ferritin in Alzheimer's Diseased Brains," <i>J. Neurosci. Res.</i> 31:75-83, Wiley-Liss, Inc. (1992).
1	AS	11	Connor, J.R., <i>et al.</i> , "Ceruloplasmin levels in the human superior temporal gyrus in aging and Alzheimer's disease," <i>Neurosci. Lett.</i> 159:88-90, Elsevier Scientific Publishers Ireland Ltd. (1993).
W	AT	11	Coyle, J.T., and Puttfarcken, P., "Oxidative Stress, Glutamate, and Neurodegenerative Disorders," <i>Science</i> 262:689-695, American Association for the Advancement of Science (1993).

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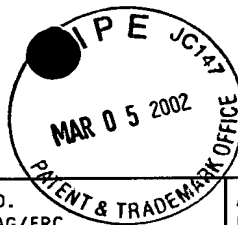
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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

lce	AR	12	Cuajungco, M.P. and Lees, G.J., "Zinc and Alzheimer's disease: is there a direct link?," <i>Brain Res. Rev.</i> 23:219-236, Elsevier Science B.V. (April 1997).
I	AS	12	Dedman, D.J., <i>et al.</i> , "Iron and aluminum in relation to brain ferritin in normal individuals and Alzheimer's-disease and chronic renal-dialysis patients," <i>Biochem J.</i> 287:509-514, The Biochemical Society (1992).
lce	AT	12	Deibel, M.A., <i>et al.</i> , "Copper, iron, and zinc imbalances in severely degenerated brain regions in Alzheimer's disease: possible relation to oxidative stress," <i>J. Neurol. Sci.</i> 143:137-142, Elsevier Science B.V. (1996).

EXAMINER <i>lce</i> <i>Wheeler</i>	DATE CONSIDERED <i>12/16/00</i>
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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
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Bush *et al.*FILING DATE  
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## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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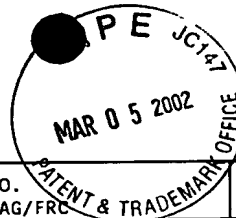
	AR	<u>13</u>	Doré, S., <i>et al.</i> , "Insulin-like growth factor I protects and rescues hippocampal neurons against $\beta$ -amyloid- and human amylin-induced toxicity," <i>Proc. Natl. Acad. Sci. USA</i> 94:4772-4777, National Academy of Sciences (April 1997).
	AS	<u>13</u>	Dyrks, T., <i>et al.</i> , "Amyloidogenicity of $\beta$ A4 and $\beta$ A4-bearing Amyloid Protein Precursor Fragments by Metal-catalyzed Oxidation," <i>J. Biol. Chem.</i> 267:18210-18217, The American Society for Biochemistry and Molecular Biology, Inc. (1992).
	AT	<u>13</u>	Ehmann W.D., <i>et al.</i> , "Brain Trace Elements in Alzheimer's Disease," <i>NeuroToxicology</i> 7:197-206, Intox Press, Inc. (1986).

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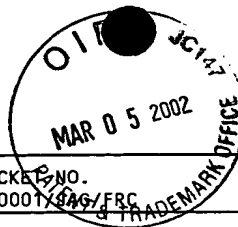
## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

26	AR	14	Esler, W.P., <i>et al.</i> , "Zinc-Induced Aggregation of Human and Rat $\beta$ -Amyloid Peptides In Vitro," <i>J. Neurochem.</i> 66:723-732, Lippincott-Raven Publishers (1996).
1	AS	14	Esler, W.P., <i>et al.</i> , "A $\beta$ deposition inhibitor screen using synthetic amyloid," <i>Nat. Biotechnol.</i> 15:258-263, Nature Publishing Company (March 1997).
10	AT	14	Fitzgerald, D.J., "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920, American Association for the Advancement of Science (1995).

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## U.S. PATENT DOCUMENTS

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	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

LC	AR	15	Folstein, M., "Nutrition and Alzheimer's Disease," <i>Nutrition Rev.</i> 55:23-25, International Life Sciences Institute (January 1997).
I	AS	15	Fraser, P.E., <i>et al.</i> , "pH-dependent structural transitions of Alzheimer amyloid peptides," <i>Biophys. J.</i> 60:1190-1201, Rockefeller University Press (1991).
CC	AT	15	Frederikse, P.H., <i>et al.</i> , "Oxidative Stress Increases Production of $\beta$ -Amyloid Precursor Protein and $\beta$ -Amyloid ( $A\beta$ ) in Mammalian Lenses, and $A\beta$ Has Toxic Effects on Lens Epithelial Cells," <i>J. Biol. Chem.</i> 271:10169-10174, The American Society for Biochemistry and Molecular Biology, Inc. (1996).

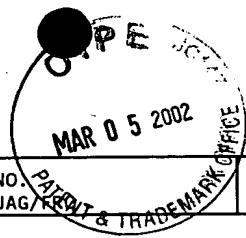
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

16	AR	16	Frederickson, C.J., "Neurobiology of Zinc and Zinc-Containing Neurons," in: <i>International Review of Neurobiology. Volume 31</i> , Smythies, J.R. and Bradley, R.J., eds., Academic Press, Inc., San Diego, CA, pp. 145-238 (1989).
16	AS	16	Frieden, E., "Ceruloplasmin: A Multi-functional Cupro-protein of Vertebrate Plasma," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Humana Press, Clifton, New Jersey, pp. 159-169 (1982).
16	AT	16	Garzon-Rodriguez, W., et al., "Soluble Amyloid A $\beta$ -(1-40) Exists as a Stable Dimer at Low Concentrations," <i>J. Biol. Chem.</i> 272:21037-21044, The American Society for Biochemistry and Molecular Biology, Inc. (August 1997).

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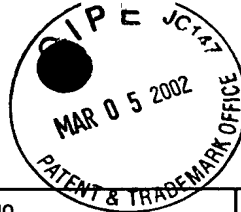
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

IC	AR	17	Giampaolo, V., <i>et al.</i> , "Copper and Inflammation," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Humana Press, Clifton, New Jersey, pp. 329-345 (1982).
I	AS	17	Giulian, D., <i>et al.</i> , "Specific Domains of $\beta$ -Amyloid from Alzheimer Plaque Elicit Neuron Killing in Human Microglia," <i>J. Neurosci.</i> 16:6021-6037, Society for Neuroscience (1996).
h	AT	17	Glenner, G.G. and Wong, C.W., "Alzheimer's Disease: Initial Report of the Purification and Characterization of a Novel Cerebrovascular Amyloid Protein," <i>Biochem. Biophys. Res. Commun.</i> 120:885-890, Academic Press, Inc. (1984).

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

20	AR	18	Golde, T.E., <i>et al.</i> , "Processing of the Amyloid Protein Precursor to Potentially Amyloidogenic Derivatives," <i>Science</i> 255:728-730, American Association for the Advancement of Science (1992).
1	AS	18	Good, P.F., <i>et al.</i> , "Selective Accumulation of Aluminum and Iron in the Neurofibrillary Tangles of Alzheimer's Disease: A Laser Microprobe (LAMMA) Study," <i>Ann. Neurol.</i> 31:286-292, American Neurological Association (1992).
16	AT	18	Goodman, Y. and Mattson, M.P., "Secreted Forms of $\beta$ -Amyloid Precursor Protein Protect Hippocampal Neurons against Amyloid $\beta$ -Peptide-Induced Oxidative Injury," <i>Exp. Neurol.</i> 128:1-12, Academic Press, Inc. (1994).

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9609.4550001/JAG/FRCAPPLICATION NO.  
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

ky	AR	19	Goodman, Y., et al., "Nordihydroguaiaretic acid protects hippocampal neurons against amyloid $\beta$ -peptide toxicity, and attenuates free radical and calcium accumulation," <i>Brain Res.</i> 654:171-176, Elsevier Science B.V. (1994).
	AS	19	Gorevic, P.D., et al., "The Biological Significance of Amyloid," <i>Ann. New York Acad. Sci.</i> 389:380-394, The New York Academy of Sciences (1982).
KL	AT	19	Grundke-Iqbal, I., et al., "Ferritin is a component of the neuritic (senile) plaque in Alzheimer dementia," <i>Acta Neuropathol.</i> 81:105-110, Springer-Verlag (1990).

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DATE CONSIDERED

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4550001/JAG/FRC	APPLICATION NO. 09/956,980
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## U.S. PATENT DOCUMENTS

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>VC</i>	AR	<u>20</u>	Gutierrez-Correa, J. and Stoppani, A.O.M., "Inactivation of Heart Dihydrolipoamide Dehydrogenase by Copper Fenton Systems. Effect of Thiol Compounds and Metal Chelators," <i>Free Rad. Res.</i> 22: 239-250, Harwood Academic Publishers GmbH (1995).
<i>I</i>	AS	<u>20</u>	Gutteridge, J.M.C. and Wilkins, S., "Copper Salt-Dependent Hydroxyl Radical Formation Damage to Proteins Acting as Antioxidants," <i>Biochim. Biophys. Acta</i> 759:38-41, Elsevier Science B.V. (1983).
<i>W</i>	AT	<u>20</u>	Haass, C., <i>et al.</i> , "Amyloid $\beta$ -peptide is produced by cultured cells during normal metabolism," <i>Nature</i> 359:322-325, Macmillan Journals Ltd. (1992).

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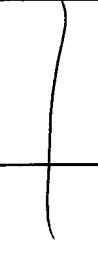

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	AN						Yes No
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>21</u>	Haley, J.V., "Zinc Sulfate and Wound Healing," <i>J. Surg. Res.</i> 27:168-174, Academic Press, Inc. (1979).
	AS	<u>21</u>	Halliwell, B. and Gutteridge, J.M.C., "Oxygen toxicity, oxygen radicals, transition metals and disease," <i>Biochem. J.</i> 219:1-14, The Biochemical Society (1984).
	AT	<u>21</u>	Halliwell, B., "Reactive Oxygen Species and the Central Nervous System," <i>J. Neurochem.</i> 59:1609-1623, Raven Press, Ltd. (1992).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

IC	AR	22	Han, J.C. and Han, G.Y., "A Procedure for Quantitative Determination of Tris(2-carboxyethyl)phosphine, an Odorless Reducing Agent More Stable and Effective Than Dithiothreitol," <i>Anal. Biochem.</i> 220:5-10, Academic Press, Inc. (1994).
I	AS	22	Han, J., <i>et al.</i> , "Quantitation of Hydrogen Peroxide Using Tris(2-carboxyethyl)phosphine," <i>Anal. Biochem.</i> 234:107-109, Academic Press, Inc. (1996).
IC	AT	22	Hansen, M.B., <i>et al.</i> , "Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill," <i>J. Immunol. Meth.</i> 119:203-210, Elsevier Science B.V. (1989).

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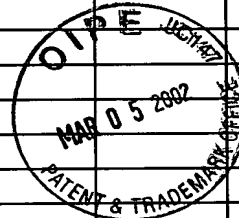
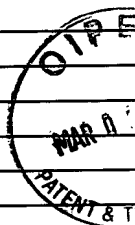
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

24	AR	23	Harman, D., "Aging: A Theory Based on Free Radical and Radiation Chemistry," <i>J. Gerontology</i> 2:298-300, Gerontological Society of America (1956).
1	AS	23	Harris, M.E., <i>et al.</i> , "Direct Evidence of Oxidative Injury Produced by the Alzheimer's $\beta$ -Amyloid Peptide (1-40) in Cultured Hippocampal Neurons," <i>Exp. Neurol.</i> 131:193-202, Academic Press, Inc. (1995).
16	AT	23	Hensley, K., <i>et al.</i> , "A model for $\beta$ -amyloid aggregation and neurotoxicity based on free radical generation by the peptide: Relevance to Alzheimer disease," <i>Proc. Natl. Acad. Sci.</i> 91:3270-3274, National Academy of Sciences (1994).

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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

Kc	AR	24	Hensley, K., <i>et al.</i> , "Brain Regional Correspondence Between Alzheimer's Disease Histopathology and Biomarkers of Protein Oxidation," <i>J. Neurochem.</i> 65:2146-2156, Lippincott-Raven Publishers (1995).
I	AS	24	Hensley, K., <i>et al.</i> , "Reactive Oxygen Species as Causal Agents in the Neurotoxicity of the Alzheimer's Disease-Associated Amyloid Beta Peptide," <i>Ann N. Y. Acad. Sci.</i> 786:120-134, The New York Academy of Sciences (1996).
Kc	AT	24	Hesse, L., <i>et al.</i> , "The $\beta$ A4 amyloid precursor protein binding to copper," <i>FEBS Lett.</i> 349:109-116, Elsevier Science (1994).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

16	AR	25	Hilbich, C., <i>et al.</i> , "Aggregation and Secondary Structure of Synthetic Amyloid $\beta$ A4 Peptides of Alzheimer's Disease," <i>J. Mol. Biol.</i> 218:149-163, Academic Press Limited (1991).
1	AS	25	Hilbich, C., <i>et al.</i> , "Substitutions of Hydrophobic Amino Acids Reduce the Amyloidogenicity of Alzheimer's Disease $\beta$ A4 Peptides," <i>J. Mol. Biol.</i> 228:460-473, Academic Press Limited (1992).
16c	AT	25	Hsu, J.M., <i>et al.</i> , "Zinc Deficiency and Incorporation of $^{14}$ C-labeled Methionine into Tissue Proteins in Rats," <i>J. Nutrition</i> 99:425-432, American Institute of Nutrition (1969).

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT				ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
				APPLICANT Bush <i>et al.</i>			
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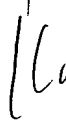
  

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>26</u>	Huang, X., <i>et al.</i> , "Zinc-induced Alzheimer's A $\beta$ 1-40 Aggregation Is Mediated by Conformational Factors," <i>J. Biol. Chem.</i> 272:26464-26470, The American Society for Biochemistry and Molecular Biology, Inc. (October 1997).
	AS	<u>26</u>	Huang, X., <i>et al.</i> , "The A $\beta$ Peptide of Alzheimer's Disease Directly Produces Hydrogen Peroxide through Metal Ion Reduction," <i>Biochem.</i> 38:7609-7616, The American Chemical Society (June 1999).
	AT	<u>26</u>	Ida, N., <i>et al.</i> , "Analysis of Heterogeneous BA4 Peptides in Human Cerebrospinal Fluid and Blood by a Newly Developed Sensitive Western Blot Assay," <i>J. Biol. Chem.</i> 271:22908-22914, The American Society for Biochemistry and Molecular Biology, Inc. (1996).

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				APPLICANT Bush <i>et al.</i>			
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	27	Jarrett, J.T. and Lansbury, Jr., P.T., "Amyloid Fibril Formation Requires a Chemically Discriminating Nucleation Event: Studies of an Amyloidogenic Sequence from the Bacterial Protein OsmB," <i>Biochemistry</i> 31:12345-12352, The American Chemical Society (1992).
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	AT	27	Johnstone, E.M., <i>et al.</i> , "Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis," <i>Mol. Brain Res.</i> 10:299-305, Elsevier Science B.V. (1991).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
16c	AR	28	Joshi, J.G., "Iron and Aluminum Homeostasis in Neural Disorders," <i>Environ. Health Persp.</i> 102:207-213, National Institute of Environmental Health Sciences (1994).
1	AS	28	Kang, J., <i>et al.</i> , "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325: 733-736, Macmillan Journals Ltd. (1987).
16c	AT	28	Kawahara, M., <i>et al.</i> , "Alzheimer's Disease Amyloid $\beta$ -Protein Forms $Zn^{2+}$ -Sensitive, Cation-Selective Channels Across Excised Membrane Patches from Hypothalamic Neurons," <i>Biophys. J.</i> 73:67-75, The Biophysical Society (July 1997).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
<div style="font-size: 2em; margin: 0;">76</div>	AR	29	Kennard, M.L., <i>et al.</i> , "Serum levels of the iron binding protein p97 are elevated in Alzheimer's disease," <i>Nature Med.</i> 2:1230-1235, Nature Publishing Company (1996).				
	AS	29	Kidani, Y., <i>et al.</i> , "Mass spectrometry of 5-chloro-7-iodo-8-quinolinol metal chelates," <i>Jpn. Analyst</i> 23:1375-1378, Nippon Bunseki Kagakkai (1974).				
	AT	29	Kirschner, D.A., <i>et al.</i> , "Synthetic peptide homologous to $\beta$ protein from Alzheimer disease forms amyloid-like fibrils in vitro," <i>Proc. Natl. Acad. Sci. USA</i> 84:6953-6957, National Academy of Sciences (1987).				
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	AN						Yes No
	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	30	Kirshenbaum, K. and Daggett, V., "pH-Dependent Conformations of the Amyloid $\beta$ (1-28) Peptide Fragment Explored Using Molecular Dynamics," <i>Biochemistry</i> 34:7629-7639, The American Chemical Society (1995).
	AS	30	Kisilevsky, R., "Inflammation-Associated Amyloidogenesis," <i>Mol. Neurobiol.</i> 8:65-66, Humana Press Inc. (1994).
	AT	30	Kisilevsky, R., "Amyloidosis: A Familiar Problem in the Light of Current Pathogenetic Developments," <i>Lab. Invest.</i> 49:381-390, International Academy of Pathology (1983).

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	APPLICANT Bush <i>et al.</i>	
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	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

W	AR	31	Koh, J.Y. and Choi, D.W., "Quantitative determination of glutamate mediated cortical neuronal injury in cell culture by lactate dehydrogenase efflux assay," <i>J. Neurosci. Meth.</i> 20:83-90, Elsevier Science B.V. (1987).
I	AS	31	Kotaki, H., <i>et al.</i> , "Intestinal Absorption and Metabolism of Clloquinol in the Rat," <i>J. Pharm. Dyn.</i> 6:881-887, Pharmaceutical Society of Japan (1983).
K	AT	31	Kuo, Y.-M., <i>et al.</i> , "Water-soluble A $\beta$ (N-40, N-42) Oligomers in Normal and Alzheimer Disease Brains," <i>J. Biol. Chem.</i> 271:4077-4081, The American Society for Biochemistry and Molecular Biology, Inc. (1996).

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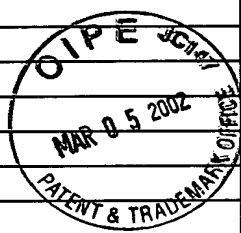
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				APPLICANT Bush <i>et al.</i>		RECEIVED MAR 08 2002 TECH CENTER 600/2900	
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	AM						Yes No
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	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
16	AR	32	Landers, J.W. and Zak, B., "Determination of Serum Copper and Iron in a Single Small Sample," <i>Am. J. Clin. Pathol.</i> 29:590-592, The Williams & Wilkins Company (1958).				
1	AS	32	Lindeman, R.D., <i>et al.</i> , "Myocardial zinc metabolism in experimental myocardial infarction," <i>J. Lab. Clin. Med.</i> 81:194-204, Central Society for Clinical Research (1973).				
16	AT	32	Linert, W., <i>et al.</i> , "Dopamine, 6-hydroxydopamine, iron, and dioxygen--their mutual interactions and possible implication in the development of Parkinson's disease," <i>Biochim. Biophys. Acta</i> 1316:160-168, Elsevier Science B.V. (1996).				
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

26	AR	33	Lockhart B.P., <i>et al.</i> , "Inhibitors of free radical formation fail to attenuate direct beta-amyloid <sub>25-35</sub> peptide-mediated neurotoxicity in rat hippocampal cultures," <i>J. Neurosci. Res.</i> 39:494-505, Wiley-Liss, Inc. (1994).
1	AS	33	Lodemann, E., "D-Penicillamin. Vom Baustein des Penicillins zum vielseitigen Pharmakon," <i>Naturwissenschaften</i> 66:462-466, Springer-Verlag (1979).
6	AT	33	Lodemann, E., "D-Penicillamine. Once a constituent of penicillin, now a potent drug," <i>CAPLUS Database Accession No. 1980:12</i> , Chemical Abstracts Service, (1980).

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	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	34	Lohr, J.B., "Oxygen Radicals and Neuropsychiatric Illness," <i>Arch. Gen. Psychiatry</i> 48:1097-1106, American Medical Association (1991).				
	AS	34	Maggio, J.E., <i>et al.</i> , "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1921, American Association for the Advancement of Science (1995).				
	AT	34	Mantyh, P.W., <i>et al.</i> , "Aluminum, Iron, and Zinc Ions Promote Aggregation of Physiological Concentrations of $\beta$ -Amyloid Peptide," <i>J. Neurochem.</i> 61:1171-1174, Raven Press, Ltd. (1993).				
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FORM PTO-1449  
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
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APPLICATION NO.  
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Bush *et al.*

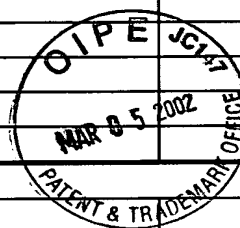
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	AN						Yes No
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	AP						Yes No

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166	AR	35	Markesbery, W.R., "Oxidative Stress Hypothesis in Alzheimer's Disease," <i>Free Rad. Biol. Med.</i> 23:134-147, Elsevier Science Inc. (July 1997).
1	AS	35	Markesbery, W.R. and Ehmann, W.D., "Chapter 22. Brain Trace Elements in Alzheimer Disease," in: <i>Alzheimer Disease</i> , Terry, R.D., <i>et al.</i> , eds., Raven Press, Ltd., New York, New York, pp.353-367 (1994).
166	AT	35	Martins, R.N., <i>et al.</i> , "Increased Cerebral Glucose-6-Phosphate Dehydrogenase Activity in Alzheimer's Disease May Reflect Oxidative Stress," <i>J. Neurochem.</i> 46:1042-1045, Raven Press (1986).

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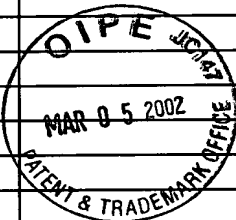
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

lc	AR	36	Masters, C.L., <i>et al.</i> , "Amyloid plaque core protein in Alzheimer disease and Down syndrome," <i>Proc. Natl. Acad. Sci. USA</i> 82:4245-4249, National Academy of Sciences (1985).
lc	AS	36	Masters, C.L., <i>et al.</i> , "Neuronal origin of a cerebral amyloid: neurofibrillary tangles of Alzheimer's disease contain the same protein as the amyloid of plaque cores and blood vessels," <i>EMBO J.</i> 4:2757-2763, IRL Press Limited (1985).
lc	AT	36	Maury, C.P.J., "Biology of Disease: Molecular Pathogenesis of $\beta$ -Amyloidosis in Alzheimer's Disease And Other Cerebral Amyloidoses," <i>Lab. Invest.</i> 72:4-16, The United States and Canadian Academy of Pathology, Inc. (1995).

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	AP					Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

26	AR	37	McGeer, P.L. and McGeer, E.G., "The inflammatory response system of brain: implications for therapy of Alzheimer and other neurodegenerative diseases," <i>Brain Res. Rev.</i> 21:195-218, Elsevier Science B.V. (1995).
1	AS	37	McKeon-O'Mally, C., <i>et al.</i> , "Potential Therapeutic Targets for Alzheimer's Disease," <i>Emerging Therapeutic Targets</i> 2:157-179, Ashley Publications Ltd. (February 1998).
16	AT	37	McLachlan, D.R.C., <i>et al.</i> , "Intramuscular desferrioxamine in patients with Alzheimer's disease," <i>Lancet</i> 337:1304-1308, Williams & Wilkins (1991).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
16	AR	38	Mecocci, P., <i>et al.</i> , "Oxidative Damage to Mitochondrial DNA Shows Marked Age-dependent Increases in Human Brain," <i>Ann. Neurol.</i> 34:609-616, American Neurological Association (1993).
1	AS	38	Menkin, V., "Studies on Inflammation. X. The Cytological Picture of an Inflammatory Exudate in Relation to its Hydrogen Ion Concentration," <i>Am. J. Pathol.</i> 10:193-210, The American Association of Pathologists and Bacteriologists (1934).
16	AT	38	Michikawa, M., <i>et al.</i> , "Oxygen Radical-Induced Neurotoxicity in Spinal Cord Neuron Cultures," <i>J. Neurosci. Res.</i> 37:62-70, Wiley-Liss, Inc. (1994).

EXAMINER <div style="text-align: center;">16e</div>	DATE CONSIDERED <div style="text-align: center;">6-16-02</div>
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
		APPLICANT Bush <i>et al.</i>			
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	AM						Yes No
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
Kc	AR	39	Milanino, R., <i>et al.</i> , "Copper and the Inflammatory Process," <i>Advances in Inflammation Research</i> 1:281-291, Raven Press (1979).
	AS	39	Moir, R.D., <i>et al.</i> , "Relative Increase in Alzheimer's Disease of Soluble Forms of Cerebral A $\beta$ Amyloid Protein Precursor Containing the Kunitz Protease Inhibitory Domain," <i>J. Biol. Chem.</i> 273:5013-5019, The American Society for Biochemistry and Molecular Biology, Inc. (February 1998).
Kc	AT	39	Mok, S.S., <i>et al.</i> , "A Novel Metalloprotease in Rat Brain Cleaves the Amyloid Precursor Protein of Alzheimer's Disease Generating Amyloidogenic Fragments," <i>Biochemistry</i> 36:156-163, The American Chemical Society (January 1997).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	40	Multhaup, G., <i>et al.</i> , "Interaction between the zinc(II) and the heparin binding site of the Alzheimer's disease $\beta$ A4 amyloid precursor protein (APP)," <i>FEBS Lett.</i> 355:151-154, Elsevier Science (1994).
	AS	40	Multhaup, G., <i>et al.</i> , "The Amyloid Precursor Protein of Alzheimer's Disease in the Reduction of Copper(II) to Copper (I)," <i>Science</i> 271:1406-1409, American Association for the Advancement of Science (1996).
	AT	40	Münch, G., <i>et al.</i> , "Advanced glycation endproducts in ageing and Alzheimer's disease," <i>Brain Res. Rev.</i> 23:134-143, Elsevier Science B.V. (February 1997).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	41	Nakada, T. and Kwee, I.L., "Guanidinoethane sulfate: brain pH alkaline shifter," <i>NeuroReport</i> 4:1035-1038, Rapid Communications of Oxford Ltd. (1993).
	AS	41	Okada, H., <i>et al.</i> , "Effects of Metal-Containing Drugs Taken Simultaneously with Clloquinol Upon Clinical Features of SMON," <i>J. Toxicol. Sci.</i> 9:327-341, Doku Sayo Kenkyukai (1984).
	AT	41	Owen, C.A., Jr., "Uptake of <sup>67</sup> Cu by Ceruloplasmin In Vitro (38878)," <i>Proc. Soc. Exp. Biol. Med.</i> 149:681-682, Academic Press, Inc. (1975).

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	AM						Yes No
	AN						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	42	Padmanabhan, G., <i>et al.</i> , "Clioquinol," in: <i>Analytical Profiles of Drug Substances</i> . vol. 18, Florey, K., ed., Academic Press, Inc., San Diego, California, pp. 57-90 (1989).
	AS	42	Pepys, M.B. and Baltz, M.L., "Acute Phase Proteins with Special Reference to C-Reactive Protein and Related Proteins (Pentaxins) and Serum Amyloid A Protein," <i>Adv. Immunol.</i> 34:141-212, Academic Press, Inc. (1983).
	AT	42	Pérez, A.A., <i>et al.</i> , "Alzheimer Amyloids Aβ1-40 and Aβ1-42 are Differentially Degraded by Insulin Degrading Enzyme (IDE) From Human Brain," <i>Soc. Neurosci. Abstracts</i> 23:821, Abs. No. 321.13, Society for Neuroscience (October 1997).

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INFORMATION DISCLOSURE STATEMENT

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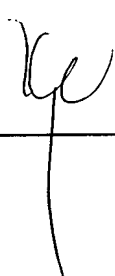
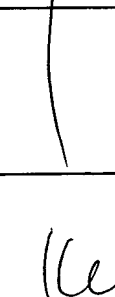

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	AL						Yes No
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>43</u>	Peters, G. and Rodgers, M.A.J., "Single-Electron Transfer from NADH Analogues to Singlet Oxygen," <i>Biochim. Biophys. Acta</i> 637:43-52, Elsevier/North-Holland Biomedical Press (1981).
	AS	<u>43</u>	Pierce, J.E.S., <i>et al.</i> , "Immunohistochemical Characterization of Alterations in the Distribution of Amyloid Precursor Proteins and $\beta$ -Amyloid Peptide after Experimental Brain Injury in the Rat," <i>J. Neurosci.</i> 16:1083-1090, Society for Neuroscience (1996).
	AT	<u>43</u>	Potempa, L.A., <i>et al.</i> , "Effect of Divalent Metal Ions and pH upon the Binding Reactivity of Human Serum Amyloid P Component, a C-reactive Protein Homologue, for Zymosan," <i>J. Biol. Chem.</i> 260:12142-12147, The American Society for Biological Chemists, Inc. (1985).

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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
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	AM						Yes No
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KE	AR	44	Richardson, J.S., <i>et al.</i> , "On the Possible Role of Iron-Induced Free Radical Peroxidation in Neural Degeneration in Alzheimer's Disease," <i>Ann. N.Y. Acad. Sci.</i> 648:326-327, The New York Academy of Sciences (1992).
I	AS	44	Roberts, G.W., <i>et al.</i> , "βA4 amyloid protein deposition in brain after head trauma," <i>Lancet</i> 338:1422-1423, Williams & Wilkins (1991).
16	AT	44	Robinson, S.R., <i>et al.</i> , "Most amyloid plaques contain ferritin-rich cells," <i>Alzheimer's Res.</i> 1:191-195, Rapid Science Publishers (1995).

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT				ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
				APPLICANT Bush <i>et al.</i>		RECEIVED MAR 06 2002 TECH CENTER 15002900	
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	<u>45</u>	Rogers, J., <i>et al.</i> , "Clinical trial of indomethacin in Alzheimer's disease," <i>Neurology</i> 43:1609-1611, Lippincott-Raven (1993).				
	AS	<u>45</u>	Roher, A.E., <i>et al.</i> , "Morphology and Toxicity of A $\beta$ -(1-42) Dimer Derived from Neuritic and Vascular Amyloid Deposits of Alzheimer's Disease," <i>J. Biol. Chem.</i> 271:20631-20635, The American Society for Biochemistry and Molecular Biology, Inc. (1996).				
	AT	<u>45</u>	Rosen, D., <i>et al.</i> , "Mutations in Cu/Zn superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis," <i>Nature</i> 364:362, Macmillan Journals Ltd. (1993).				
EXAMINER <u>llc</u>					DATE CONSIDERED <u>6-16-01</u>		
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.							

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>ku</i>	AR	<u>46</u>	Rumble, B., <i>et al.</i> , "Amyloid A4 Protein and Its Precursor in Down's Syndrome and Alzheimer's Disease," <i>New Eng. J. Med.</i> 320:1446-1452, Massachusetts Medical Society (1989).
<i>l</i>	AS	<u>46</u>	Sadowski, M., <i>et al.</i> , "Astrocyte and microglia reaction in Alzheimer's disease in the hippocampal formation- a quantitative analysis," <i>Alzheimer's Res.</i> 1:71-76, Rapid Science Publishers (1995).
<i>ll</i>	AT	<u>46</u>	Sano, M., <i>et al.</i> , "A Controlled Trial of Selegiline, Alpha-Tocopherol, or Both as Treatment for Alzheimer's Disease," <i>N. Engl. J. Med.</i> 336:1216-1222, Massachusetts Medical Society (April 1997).

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	AM						Yes No
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
166	AR	47	Sayre, L.M., "Alzheimer's Precursor Protein and the Use of Bathocuproine for Determining Reduction of Copper(II)," <i>Science</i> 274:1933-1934, American Association for the Advancement of Science (1996).
1	AS	47	Schnabel, J., "New Alzheimer's Therapy Suggested," <i>Science</i> 260:1719-1720, American Association for the Advancement of Science (1993).
166	AT	47	Schrader-Fiscer, G. and Paganetti, P.A., "Effect of alkalizing agents on the processing of the $\beta$ -amyloid precursor protein," <i>Brain Res.</i> 716:91-100, Elsevier Science B.V. (1996).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
X	AR	48	Schubert, D. and Chevion, M., "The Role of Iron in Beta Amyloid Toxicity," <i>Biochem. Biophys. Res. Comm.</i> 216:702-707, Academic Press, Inc. (1995).
	AS	48	Selkoe, D.J., "Cell Biology of the Amyloid $\beta$ -protein Precursor and the Mechanism of Alzheimer's Disease," <i>Ann. Rev. Cell Biol.</i> 10:373-403, Annual Reviews, Inc. (1994).
W	AT	48	Seubert, P., <i>et al.</i> , "Isolation and quantification of soluble Alzheimer's $\beta$ -peptide from biological fluids," <i>Nature</i> 359:325-327, Macmillan Journals Ltd. (1992).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>Re</i>	AR	49	Shiraki, H., "Neuropathological aspects of the etiopathogenesis of subacute myelo-optico-neuropathy (SMON)," in: <i>Handbook of Clinical Neurology</i> . vol. 37, Vinken, P.J. and Bruyn, G.W., eds., North-Holland Publishing Company, Amsterdam, The Netherlands, pp. 141-197 (1979).
<i>I</i>	AS	49	Shivers, B.D., <i>et al.</i> , "Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact," <i>EMBO J.</i> 7:1365-1370, IRL Press Limited (1988).
<i>Re</i>	AT	49	Shoji, M., <i>et al.</i> , "Production of the Alzheimer Amyloid $\beta$ Protein by Normal Proteolytic Processing," <i>Science</i> 258:126-129, American Association for the Advancement of Science (1992).

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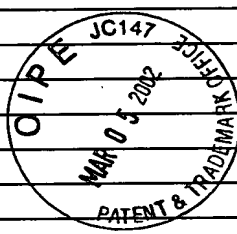
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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

Ke	AR	50	Sisodia, S.S., <i>et al.</i> , "Cellular and molecular biology of Alzheimer's disease and animal models," <i>Neuroimaging Clinics of North America</i> 5:59-68, W.B. Saunders Co. (1995).
I	AS	50	Skinner, M., <i>et al.</i> , "Observations on the amyloid-degrading activity of serum and its relationship to human neutrophil elastase," <i>Chemical Abstracts</i> 101:453, Abstract No. 101:208677n, The American Chemical Society (1984).
lu	AT	50	Smalheiser, N.R. and Swanson, D.R., "Indomethacin and Alzheimer's disease," <i>Neurology</i> 46:583, American Academy of Neurology (1996).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<div style="font-size: 2em; margin-top: 20px;">K</div>	AR	51	Smith, C. and Anderton, B.H., "The molecular pathology of Alzheimer's disease: are we any closer to understanding the neurodegenerative process?," <i>Neuropathol. Appl. Neurobiol.</i> 20:322-38, Blackwell Scientific Publications (1994).
<div style="font-size: 2em; margin-top: 20px;">I</div>	AS	51	Smith, M.A., <i>et al.</i> , "Radical AGEing in Alzheimer's disease," <i>Trends Neurosci.</i> 18:172-176, Elsevier Science Ltd. (1995).
<div style="font-size: 2em; margin-top: 20px;">u</div>	AT	51	Smith, M.A., <i>et al.</i> , "Oxidative damage in Alzheimer's," <i>Nature</i> 382:120-121, Macmillan Journals Ltd. (1996).

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT				ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
				APPLICANT Bush <i>et al.</i>			
				FILING DATE September 21, 2001		GROUP 1614	

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
Kc	AR	52	Smith, M.A., <i>et al.</i> , "Iron accumulation in Alzheimer disease is a source of redox-generated free radicals," <i>Proc. Natl. Acad. Sci. USA</i> 94:9866-9868, National Academy of Sciences (September 1997).
I	AS	52	Sobue, I., "Clinical aspects of subacute myelo-optico-neuropathy (SMON)," in: <i>Handbook of Clinical Neurology. Intoxications of the Nervous System Part II</i> , Vinken, P.J. and Bruyn, G. W., eds., North-Holland Publishing Company, Amsterdam, The Netherlands, pp.115-139 (1979).
Kc	AT	52	Soto, C., <i>et al.</i> , " $\beta$ -sheet breaker peptides inhibit fibrillogenesis in a rat brain model of amyloidosis: Implications for Alzheimer's therapy," <i>Nature Med.</i> 4:822-826, Nature Publishing Company (July 1998).

EXAMINER <span style="float: right;">Kc</span>	DATE CONSIDERED <span style="float: right;">6.16.02</span>
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	53	Soto, C., <i>et al.</i> , "Inhibition of Alzheimer's Amyloidosis by Peptides That Prevent $\beta$ -Sheet Conformation," <i>Biochem. Biophys. Res. Comm.</i> 226:672-680 (1996).
	AS	53	Soto, C., <i>et al.</i> , "Structural Determinants of the Alzheimer's Amyloid $\beta$ -Peptide," <i>J. Neurochem.</i> 63:1191-1198, Raven Press, Ltd. (1994).
	AT	53	Stankovic, A. and Mitrovic, D.R., "Aluminum Salts Stimulate Luminol-Enhanced Chemiluminescence Production by Human Neutrophils," <i>Free Rad. Res. Comms.</i> 14:47-55, Harwood Academic Publishers GmbH (1991).

EXAMINER 	DATE CONSIDERED 6-16-07
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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>				ATTY. DOCKET NO. 0609.4550001/JAG/FRC		APPLICATION NO. 09/956,980	
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
<div style="text-align: center;"> </div>	AR	<u>54</u>	Sue, Y.-J., <i>et al.</i> , "Efficacy of Magnesium Citrate Cathartic in Pediatric Toxic Ingestions," <i>Annals of Emergency Medicine</i> 24:709-712, American College of Emergency Physicians (1994).				
	AS	<u>54</u>	Suzuki, N., <i>et al.</i> , "An Increased Percentage of Long Amyloid $\beta$ -Protein Secreted by Familial Amyloid $\beta$ -Protein Precursor (BAPP <sub>717</sub> ) Mutants," <i>Science</i> 264:1336-1340, American Association for the Advancement of Science (1994).				
	AT	<u>54</u>	Tanzi, R.E., <i>et al.</i> , "The Wilson disease gene is a copper transporting ATPase with homology to the Menkes disease gene," <i>Nat. Genet.</i> 5:344-350, Nature Publishing Co. (1993).				
EXAMINER					DATE CONSIDERED 6-16-02		
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>X</i> <i>lu</i>	AR	55	Tanzi, R.E., <i>et al.</i> , "Amyloid $\beta$ Protein Gene: cDNA, mRNA Distribution, and Genetic Linkage Near the Alzheimer Locus," <i>Science</i> 235:880-884, American Association for the Advancement of Science (1987).
<i>1</i>	AS	55	Tamura, Z., "Clinical Chemistry of Clioquinol," <i>Jpn. J. Med. Sci. Biol.</i> 28:69-77, The National Institute of Health (1975).
<i>16</i>	AT	55	Tateishi, J., <i>et al.</i> , "Strain-differences in dogs for neurotoxicity of clioquinol," <i>Lancet</i> 1:1289-1290, Little, Brown and Company (1972).

EXAMINER <i>X</i> <i>lu</i>	DATE CONSIDERED 6-16-02
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	56	Tateishi, J., <i>et al.</i> , "Neurotoxicity of Clloquinol in Laboratory Animals," <i>Lancet</i> 2:1095, Massachusetts Medical Society (1972).
	AS	56	Tateishi, J., <i>et al.</i> , "Myeloneuropathy in dogs induced by iodoxyquinoline," <i>Neurology</i> 22:702-709, American Academy of Neurology (1972).
	AT	56	Tateishi, J., <i>et al.</i> , "Autoradiographic Distribution of <sup>131</sup> I-Clloquinol in Canine and Feline," <i>Folia Psychiatrica et Neurologica Japonica</i> 26:159-164, The Japanese Society of Psychiatry and Neurology (1972).

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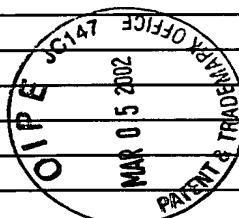
## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
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## U.S. PATENT DOCUMENTS

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

ke	AR	57	Tateishi, J., <i>et al.</i> , "Neurotoxicity of Clioquinol. Part III: Autoradiographic Distribution of Radioactive Clioquinol in Several Species of Animals," <i>Psychiat. Neurol. Jap.</i> 75:187-196, The Japanese Society of Psychiatry and Neurology (1973).
I	AS	57	Tateishi, J., <i>et al.</i> , "Neurotoxicity of Clioquinol. Part III: Autoradiographic Distribution of Radioactive Clioquinol in Several Species of Animals," <i>Database CAPLUS Accession No.</i> 1973:500388, Chemical Abstracts Service (1973).
ke	AT	57	Tateishi, J., <i>et al.</i> , "Experimental Myelo-optic Neuropathy Induced by Clioquinol," <i>Acta Neuropath. (Berl.)</i> 24:304-320, Springer-Verlag (1973).

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				APPLICANT Bush <i>et al.</i>			
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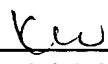
  

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>58</u>	Teller, J.K., <i>et al.</i> , "Presence of soluble amyloid $\beta$ -peptide precedes amyloid plaque formation in Down's Syndrome," <i>Nature Med.</i> 2:93-95, Nature Publishing Company (1996).
	AS	<u>58</u>	Terhune, M.W. and Sandstead, H.H., "Decreased RNA Polymerase Activity in Mammalian Zinc Deficiency," <i>Science</i> 177:68-69, American Association for the Advancement of Science (1972).
	AT	<u>58</u>	Terry, R.D., <i>et al.</i> , "Physical Basis of Cognitive Alterations in Alzheimer's Disease: Synapse Loss Is the Major Correlate of Cognitive Impairment," <i>Ann. Neurol.</i> 30:572-580, American Neurological Association (1991).

EXAMINER 	DATE CONSIDERED <u>6-16-02</u>
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				APPLICANT Bush <i>et al.</i>			
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	AM						Yes No
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
10	AR	59	Thomas, T., <i>et al.</i> , " $\beta$ -Amyloid-mediated vasoactivity and vascular endothelial damage," <i>Nature</i> 380:168-171, Macmillan Journals Ltd. (1996).
1	AS	59	Thompson, C.M., <i>et al.</i> , "Regional Brain Trace-Element Studies in Alzheimer's Disease," <i>NeuroToxicol.</i> 9:1-8, Intox Press, Inc. (1988).
16	AT	59	Tomiyama, T., <i>et al.</i> , "Rifampicin Prevents the Aggregation and Neurotoxicity of Amyloid $\beta$ Protein <i>In Vitro</i> ," <i>Biochem. Biophys. Res. Comm.</i> 204:76-83, Academic Press, Inc. (1994).

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## U.S. PATENT DOCUMENTS

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	AN						Yes No
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>60</u>	Tomiyama, T., <i>et al.</i> , "Inhibition of Amyloid $\beta$ Protein Aggregation and Neurotoxicity by Rifampicin," <i>J. Biol. Chem.</i> 271:6839-6844, The American Society for Biochemistry and Molecular Biology, Inc. (1996).
AS	<u>60</u>	Tomski, S.J. and Murphy, R.M., "Kinetics of Aggregation of Synthetic $\beta$ -Amyloid Peptide," <i>Arch. Biochem. Biophys.</i> 294:630-638, Academic Press, Inc. (1992).
AT	<u>60</u>	Treuhart, P.S. and McCarty, D.J., "Synovial Fluid pH, Lactate, Oxygen and Carbon Dioxide Partial Pressure in Various Joint Diseases," <i>Arthritis Rheum.</i> 14:475-484, Harper & Row (1971).

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	AR	<u>61</u>	Uchida, K. and Kawakishi, S., "Identification of Oxidized Histidine Generated at the Active Site of Cu,Zn-Superoxide Dismutase Exposed to H <sub>2</sub> O <sub>2</sub> . Selective Generation Of 2-Oxo-Histidine At The Histidine 118," <i>J. Biol. Chem.</i> 269:2405-2410, The American Society for Biochemistry and Molecular Biology, Inc. (1994).
	AS	<u>61</u>	Van Nostrand, W.E, "Zinc (II) Selectively Enhances the Inhibition of Coagulation Factor XIa by Protease Nexin-2/Amyloid $\beta$ -Protein Precursor," <i>Thrombosis Res.</i> 78:43-53, Elsevier Science Ltd. (1995).
	AT	<u>61</u>	Warren, P.J., <i>et al.</i> , "The Distribution of Copper in Human Brain," <i>Brain</i> 83:709-717, Macmillan and Co., Limited (1960).

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

10	AR	62	Weismann, K. and Knudsen, L., "Effects of Penicillamine and Hydroxyquinoline on Absorption of Orally Ingested <sup>65</sup> Zinc in the Rat," <i>J. Invest. Dermatol.</i> 71:242-244, The Williams & Wilkins Company (1978).
11	AS	62	Wolozin, B., <i>et al.</i> , "Participation of Presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation," <i>Science</i> 274:1710-1713, American Association for the Advancement of Science (1996).
10	AT	62	Wood, S.J., <i>et al.</i> , "Physical, Morphological and Functional Differences between pH 5.8 and 7.4 Aggregates of the Alzheimer's Amyloid Peptide A $\beta$ ," <i>J. Mol. Biol.</i> 256:870-877, Academic Press Limited (1996).

EXAMINER <i>Lew</i>	DATE CONSIDERED 6.16.07
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Bush *et al.*

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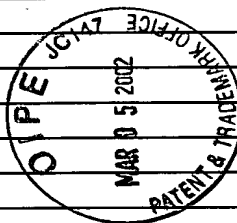
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

Ue	AR	63	Yankner, B.A., <i>et al.</i> , "Neurotrophic and Neurotoxic Effects of Amyloid $\beta$ Protein: Reversal by Tachykinin Neuropeptides," <i>Science</i> 250:279-282, American Association for the Advancement of Science (1990).
	AS	63	Yates, C.M., <i>et al.</i> , "Enzyme Activities in Relation to pH and Lactate in Postmortem Brain in Alzheimer-Type and Other Dementias," <i>J. Neurochem.</i> 55:1624-1630, Raven Press (1990).
(C)	AT	63	Yim, M.B., <i>et al.</i> , "A gain-of-function of an amyotrophic lateral sclerosis-associated Cu,Zn-superoxide dismutase mutant: An enhancement of free radical formation due to a decrease in $K_m$ for hydrogen peroxide," <i>Proc. Natl. Acad. Sci. USA</i> 93:5709-5714, National Academy of Sciences (1996).

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## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

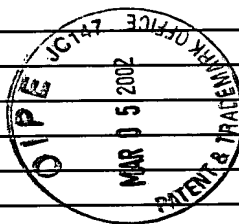
10	AR	64	Zagorski, M.G. and Barrow, C.J., "NMR Studies of Amyloid $\beta$ -Peptides: Proton Assignments, Secondary Structure, and Mechanism of an $\alpha$ -Helix $\rightarrow$ $\beta$ -Sheet Conversion for a Homologous, 28-Residue, N-Terminal Fragment," <i>Biochemistry</i> 31:5621-5631, The American Chemical Society (1992).
1	AS	64	International Search Report for International Application No. PCT/US98/04683, mailed June 19, 1998.
66	AT	64	International Search Report for International Application No. PCT/US99/05291, mailed February 21, 2000.

EXAMINER

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## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
0609.4550001/JAG/FRCAPPLICATION NO.  
09/956,980APPLICANT  
Bush *et al.*FILING DATE  
September 21, 2001GROUP  
1614

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

60	AR	65	International Search Report for International Application No. PCT/US00/11715, mailed August 30, 2000.
60	AS	65	Pending Non-Provisional U.S. Patent Application No. 09/380,704, Bush <i>et al.</i> , filed September 8, 1999.
	AT		

EXAMINER	DATE CONSIDERED
<i>[Signature]</i>	6-16-02

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